CLAIMS

What is claimed is:

1. A method of identifying whether a candidate compound is a modulator of a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or a fragment or variant thereof, wherein the receptor couples to a G protein, comprising the steps of:

(a') contacting the candidate compound with the receptor;

(b') determining whether the receptor functionality is modulated, wherein a change in receptor functionality is indicative of the candidate compound being a modulator of said GPCR.

2. A method of identifying whether a candidate compound is a modulator of cardioprotection, comprising the steps of:

(a) contacting the candidate compound with a GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(i) the polypeptide of SEQ ID NO:2;

(ii) the polypeptide of SEQ ID NO:3; and

(iii) the polypeptide of SEQ ID NO:5;

or a fragment thereof, wherein the receptor couples to a G protein; and

(b) determining whether the receptor functionality is modulated;

wherein a change in receptor functionality is indicative of the candidate compound being a modulator of cardioprotection.

3. The method of claim 1 or claim 2, wherein said receptor is recombinant.

4. The method of claim 1 or claim 2, wherein said determining is through the measurement of the level of a second messenger selected from the group consisting of cyclic AMP (cAMP), cyclic GMP (cGMP), inositol triphosphate (IP_3), diacylglycerol (DAG) and Ca^{2+}.

5. The method of claim 4, wherein said second messenger is cAMP.

6. The method of claim 5, wherein the intracellular level of cAMP is reduced.

7. The method of claim 1 or claim 2, wherein said determining is through the use of a Melanophore assay.

8. The method of claim 1 or claim 2, wherein said determining is through the measurement of GTPγS binding to membrane comprising said GPCR.

9. The method of claim 1 or claim 2, further comprising the step of comparing the modulation of the receptor caused by the candidate compound to a second modulation of the receptor caused by contacting the receptor with a known modulator of the receptor.

10. A modulator identified according to a method of claim 1 or claim 2.

11. A modulator of claim 10 selected from the group consisting of agonist, partial agonist, inverse agonist and antagonist.

12. A modulator of claim 11, wherein said modulator reduces the intracellular level of cAMP.

13. A modulator of claim 11 or claim 12, wherein said modulator is an agonist.

14. A method of modulating the activity of a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or a fragment or variant thereof, wherein the receptor couples to a G protein, comprising the step of contacting the receptor with a modulator of any one of claims 10 to 13.

15. The method of claim 14, wherein said contacting comprises administration of the modulator to a membrane comprising the receptor.

16. The method of claim 14, wherein said contacting comprises administration of the modulator to a cell or tissue comprising the receptor.

17. The method of claim 14, wherein said contacting comprises administration of the modulator to an individual comprising the receptor.

18. The method of claim 17, wherein said individual is in need of prevention of or treatment for a cardiovascular disorder selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

19. The method of claim 17, wherein said individual is in need of prevention of or treatment for an ischemic heart disease selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure.

20. The method of claim 17, wherein said individual is in need of a change in cardiovascular function selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume; and

(d) a decrease in cardiomyocyte apoptosis.

21. A method of changing cardiovascular function in an individual in need of said change, comprising contacting a therapeutically effective amount of a modulator of the second aspect with a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or an allelic variant thereof.

22. The method of claim 21, wherein said change in cardiovascular function is selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume; and

(d) a decrease in cardiomyocyte apoptosis.

23. A method of prevention of or treatment for a cardiovascular disorder in an individual in need of said change, comprising contacting a therapeutically effective amount of a modulator of

the second aspect with a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or an allelic variant thereof.

24. The method of claim 23, wherein said cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

25. A method of prevention of or treatment for an ischemic heart disease in an individual in need of said change, comprising contacting a therapeutically effective amount of a modulator of the second aspect with a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or an allelic variant thereof.

26. The method of claim 25, wherein said ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure.

27. A method of preparing a composition, comprising identifying a modulator of a **RUP41** GPCR and then admixing a carrier and the modulator, wherein the modulator is identificable by a method of claim 1 or claim 2.

28. A pharmaceutical or physiologically acceptable composition comprising, consisting essentially of, or consisting of a modulator of any one of claims 10 to 13.

29. A method of changing cardiovascular function, comprising providing or administering to an individual in need of said change said pharmaceutical or physiologically acceptable

composition of claim 28, wherein said change in cardiovascular function is selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume;. And

(d) a decrease in cardiomyocyte apoptosis.

30. A method of preventing or treating a cardiovascular disorder, comprising providing or administering to an individual in need of said treatment said pharmaceutical or physiologically acceptable composition of claim 28, wherein said cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

31. A method of preventing or treating an ischemic heart disease comprising providing or administering to an individual in need of said treatment said pharmaceutical or physiologically acceptable composition of claim 28, wherein said ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodelling; and

(c) congestive heart failure.

32. A method of using a modulator of any one of claims 10 to 13 for the preparation of a medicament for the prevention or treatment of a cardiovascular disorder in an individual, wherein said cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

33. A method of using a modulator of any one of claims 10 to 13 for the preparation of a medicament for the prevention or treatment of an ischemic heart disease in an individual, wherein said ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodelling; and

(c) congestive heart failure.

34. The method of any one of claims 17 to 26 and 29 to 33, wherein said individual is a mammal.

35. A method of making a knockout mouse, wherein said knockout mouse is predisposed to a cardiovascular disorder selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures;

comprising the step of knocking out a gene encoding the polypeptide of SEQ. ID. NO.:5.

36. A method of making a knockout mouse, wherein said knockout mouse is predisposed to an ischemic heart disease selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure;

comprising the step of knocking out a gene encoding the polypeptide of SEQ. ID. NO.:5.

37. The knockout mouse of claim 35 or claim 36.

38. A method of using the knockout mouse of claim 37 to identify whether a candidate compound has therapeutic efficacy for the prevention or treatment of a cardiovascular disorder or an ischemic heart disease.

39. A method of making a knockout rat, wherein said knockout rat is predisposed to a cardiovascular disorder selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures;

comprising the step of knocking out a gene hybridizing at high stringency to the polynucleotide of SEQ. ID. NO.:6.

40. A method of making a knockout rat, wherein said knockout rat is predisposed to an ischemic heart disease selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure;

comprising the step of knocking out a gene hybridizing at high stringency to the polynucleotide of SEQ. ID. NO.:6.

41. The knockout rat of claim 39 or claim 40.

42. A method of using the knockout rat of claim 41 to identify whether a candidate compound has therapeutic efficacy for the prevention or treatment of a cardiovascular disorder or an ischemic heart disease.

43. An isolated rat **RUP41** polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising a contiguous span of at least 75 nucleotides of SEQ ID NO:6;

(b) a polynucleotide comprising a contiguous span of at least 150 nucleotides of SEQ ID NO:6;

(c) a polynucleotide comprising a contiguous span of at least 250 nucleotides of SEQ ID NO:6;

(d) a polynucleotide comprising a contiguous span of at least 350 nucleotides of SEQ ID NO:6; and

(e) a polynucleotide comprising a contiguous span of at least 500 nucleotides of SEQ ID NO:6;

or the complement thereof.

44. A recombinant vector, said recombinant vector comprising the isolated polynucleotide of claim 43.

45. A host cell comprising the recombinant vector of claim 44.

46. A GPCR Fusion Protein construct comprising a constitutively active G protein coupled receptor and a G protein, said receptor comprising a **RUP41** polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or a fragment or variant thereof.

47. A method of identifying whether a candidate compound is a ligand of a **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:3; and

(c) the polypeptide of SEQ ID NO:5;

or a fragment or variant thereof, comprising the steps of:

(a') contacting said polypeptide with said known modulator, optionally labeled, in the presence or absence of said candidate compound;

(b') detecting the complex between said known modulator and said polypeptide; and

(c') determining whether less of said complex is formed in the presence of the compound than in the absence of the compound;

wherein said determination is indicative of the candidate compound being a ligand of said receptor.

48. A method of radioimaging, comprising providing or administering to an individual in need of said radioimaging a radiolabeled compound selected from the group consisting of a modulator of claim 2 and a ligand of claim 47.

49. A non-human mammal transgenic for a human **RUP41** GPCR, said receptor comprising a polypeptide selected from the group consisting of:

(a) the polypeptide of SEQ ID NO:2;

(b) the polypeptide of SEQ ID NO:2 wherein the phenylalanine at amino acid position 312 of SEQ ID NO:2 is substituted with lysine;

(c) the polypeptide of SEQ ID NO:3; and

(d) the polypeptide of SEQ ID NO:3 wherein the phenylalanine at amino acid position 312 of SEQ ID NO:3 is substituted with lysine.

50. A method of using the transgenic non-human mammal of claim 49 to identify whether a compound has efficacy for cardioprotection, wherein said compound is selected from the group consisting of a modulator of claim 2 and a ligand of claim 47.

51. A process for making a modulator of a **RUP41** GPCR, comprising the steps of:

(a) identifying said modulator according to the method of claim 1 or claim 2; and

(b) synthesizing the modulator identified in (a).

52. The process of claim 51, wherein said modulator is selected from the group consisting of agonist, partial agonist, inverse agonist and antagonist.

53. The process of claim 51, wherein said modulator reduces the intracellular level of cAMP.

54. The process of claim 52 or claim 53, wherein said modulator is an agonist.

55. A modulator according to any one of claims 10 to 13 for use the changing cardiovascular function.

56. The method of claim 55, wherein said change in cardiovascular function is selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume; and

(d) a decrease in cardiomyocyte apoptosis.

57. A modulator according to any one of claims 10 to 13 for use in the prevention of or treatment for a cardiovascular disorder.

58. The method of claim 57, wherein said cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

59. A modulator according to any one of claims 10 to 13 for use in the prevention of or treatment for an ischemic heart disease.

60. The method of claim 59, wherein said ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure.